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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

IN RE: BATES, James N., et al.	
	APPEAL NO. _____
SERIAL NO: 09/879,710	
FOR: S-METHYLCYSTEINE, S-ETHYL-CYSTEINE, AND RELATED S-ALKYLTHIOLS AS ANTAGONISTS TO THE EFFECTS OF S-NITROSOTHIOLS AND NITRIC OXIDE	**BRIEF ON APPEAL**
FILED: June 12, 2001	
GROUP ART UNIT: 1654	

To the Commissioner of Patents and Trademarks
Mail Stop PATENT APPEAL,
P. O. Box 1450,
Alexandria, VA 22313-1450

Dear Sirs:

Please enter the following Brief on Appeal into the record.

CERTIFICATE OF MAILING BY EXPRESS MAIL

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Betty J. Albritton

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I. INTRODUCTION

This is an appeal of the Final Rejection dated January 24, 2005, finally rejecting claims 2-8 and 10. The appealed claims 2-8 and 10 are set forth in an attached Appendix.

II. REAL PARTY OF INTEREST

The real party of interest in the present appeal is the assignee, University of Iowa Research Foundation, Oakdale Research Campus, 1000 Oakdale Campus, #214 TIC, Iowa City, Iowa 52242-5000, by an assignment from the co-inventors recorded January 22, 2002, at Reel/Frame 012536/0550.

III. RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences.

IV. STATUS OF CLAIMS

Claims 1-11 were originally submitted June 12, 2001. In an Amendment dated December 13, 2001, and in response to a restriction requirement by the Examiner, Appellant elected with traverse claims 1-8 to prosecute and withdrew claims 9-11 from consideration. Appellant further amended claims 1, 7, and 8 at this time.

In an Amendment After Final Rejection dated July 2, 2002, Appellant amended claims 7 and 8. This Amendment was refused entry in an Advisory Action dated July 19, 2002.

On August 19, 2002, Appellant filed a Notice of Appeal, and on October 15, 2002 filed its Brief on Appeal.

Instead of responding to the appeal, on January 14, 2003, the Examiner issued another Office Action rejecting claims 1-8. In an Amendment dated April 14, 2003, Appellant amended claims 2-4 and 7-8. Appellant further added claim 9.

On October 2, 2003, the Examiner issued a Notice of Abandonment, stating that no response to the January 14, 2003 Office Action had been received. On October 24, 2003, Appellant filed a Petition for Withdrawal of Abandonment enclosing proof of submission of the April 14, 2003 amendment. The Petition was granted on March 4, 2004.

On October 19, 2004, the Examiner issued an Office Action stating that Appellant's April 14, 2003 amendment submitted with its October 24, 2003 Petition was non-responsive, and gave Appellant one month or thirty days in which to respond.

On November 3, 2004, Appellant filed a response amending claims 2-4 and 7-8. Appellant further added claim 10.

Following another final rejection dated January 24, 2005, Appellant filed a Notice of Appeal dated March 4, 2005. The claims here appealed are claims 2-8 and 10.

V. STATUS OF AMENDMENTS

No Amendments were filed following the Examiner's Final Rejection dated January 24, 2005. A Notice of Appeal was timely filed on March 4, 2005.

VI. SUMMARY OF CLAIMED SUBJECT MATTER

A. Independent Claim 10

Independent claim 10 sets forth a method of counter acting the overproduction of nitric oxide which often occurs in hypotension and shock. (Spec. p. 1, lines 23-24). The method consists essentially of administering to a patient a therapeutically effective amount of an S-alkylthiol as an antagonist of S-nitrosothiols. (Spec. p. 3, lines 1-10).

VII. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

A. Claims 2, 3, 8, and 10 stand rejected under 35 U.S.C. 102(b) as being anticipated by Meisner.

B. Claims 2-8 and 10 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Meisner taken with Joullie et al. and Chemical Abstracts Registry file print.

VIII. ARGUMENT

A. Rejection Under 35 U.S.C. § 102(b), Anticipation by Meisner, U.S. Patent No. 4,772,591

Claims 2, 3, 8, and 10 were rejected under 35 U.S.C. 102(b) as being anticipated by Meisner. The Examiner argues that Meisner teaches that a composition containing among other ingredients, an anti-inflammatory substance, specifically, S-methylcysteine, is administered to a patient (see abstract, col. 5, lines 3-27, col. 6, lines 6-8 and 57-67 and the claims). The Examiner further argues that even though the composition is administered to the patient for a different reason than that disclosed in the reference, it would have been inherent to the process of Meisner that nitric oxide synthesis is inhibited since the steps of the processes (Meisner and the instant application) are the same.

1. The Law of Anticipation

A rejection for anticipation requires the presence in a single prior art reference disclosure of each and every element of the claimed invention. Lindemann Maschinenfabrik GmbH v. American Hoist & Derrick Co., 730 F.2d 1452, 221 USPQ 481, 485 (Fed. Cir. 1984). Further, the reference must generally place the needed subject matter supporting the anticipation rejection in the public domain before the date of invention. In re Zenitz, 333 F.2d 924, 142 USPQ 158, 160 (C.C.P.A. 1964). It follows from this second element that a reference does not legally anticipate the claimed subject matter if it is found not to be sufficiently enabling, in other words, if it does not place the subject matter of the claims

within the possession of the public. In re Wilder, 429 F.2d 447, 166 USPQ 545 (C.C.P.A. 1970).

2. Claims 2, 3, 8, and 10

Claim 10, from which claims 2, 3, and 8 depend, is directed to a method of counter acting the overproduction of nitric oxide, consisting essentially of: administering to a patient a therapeutically effective amount of an S-alkylthiol as an antagonist of S-nitrosothiols. Thus, by definition, the claims are limited to the administration of an S-alkylthiol and other ingredients that "do not materially affect the basic and novel characteristic(s)" of the claimed invention. MPEP § 2111.03.

By contrast, Meisner teaches a method and composition for accelerating the healing of wounds in animals and humans comprising the administration of four substances, namely:

-a source of biologically available calcium;

-ascorbic acid;

-a precursor or stimulant of epinephrine or nor-epinephrine production selected from tyrosine, and phenylalanine; and

-a mild anti-inflammatory substance selected from the anti-inflammatory members of the group consisting of simple sugars, amino sugars, amino acids, and derivatives thereof. S-methylcysteine is listed as one type of amino acid suitable for this purpose.

(Col. 2, lines 67-68 to Col. 3, lines 1-6; Col. 4, lines 60-61).

Incredibly, the Examiner argues that the limitation of "consisting essentially of" in Appellant's claim should be ignored, and interpreted to mean the same as "comprising". (January 24, 2005 Office Action, p. 3). In this regard, the Examiner argues that Appellant has not provided, "a clear indication in the specification or claims of what the basic and novel

characteristics [of the invention] are." (1/24/05 Office Action, p. 3). Hence, it is the Examiner's position that Appellant's claims should be interpreted as including all four of the required substances of Meisner. This position is not well supported or well taken.

The first paragraph of Appellant's specification states that the present invention is directed to therapeutic methods involving the administration of antagonists of S-nitrosothiols, which are naturally occurring compounds involved in the regulation of blood pressure, pain perception, control of smooth muscle tone, and numerous other functions. (Spec. p. 1, lines 5-10). In this regard, Appellant notes that nitric oxide is a major intracellular signal that causes, among other things, vasodilation. (Spec. p. 1, lines 12-15). Thus, the overproduction of nitric oxide can lead to the profound hypotension associated with septic shock, which in turn leads to hypoperfusion and organ failure, including cardiac failure. (Spec. p. 1, lines 20-30).

At the time of filing of the present application, current treatments options for hypotension or septic shock have been limited to vasoconstricting agents that have many deleterious side effects that limit their therapeutic usage. (Spec. p. 2, lines 11-16). Therefore, a primary goal of the present invention was the development of effective pharmacological treatments to counteract hypotension and shock without the deleterious side effects associated with the use of vasoconstricting agents. (Spec. p. 2, lines 11-19). It is believed that the compounds of the present invention, act as an antagonist to S-nitrosocysteine and other S-nitrosothiols. (Spec. pp. 6-7).

As already noted, Meisner requires the presence of a precursor or stimulant of epinephrine or nor-epinephrine production that is either tyrosine or phenylalanine. (Col. 3, lines 1-3). Epinephrine and norepinephrine are well known, however, to be potent vasoconstricting agents. In this regard, epinephrine stimulates α_1 and both β_1 and β_2

receptors, while norepinephrine is an α and β_1 agonist. Such compounds do not fall within the scope of claims 2-3, 8, and 10, as extensively taught by Appellant's specification, since they would "materially affect the basic and novel characteristic(s)" of the claimed invention." More specifically, since a specifically stated and primary goal of the claimed invention is to avoid the side effects associated with vasoconstricting agents, the incorporation of "a precursor or stimulant of epinephrine or nor-epinephrine" that acts as a vasoconstricting agent would counteract the specifically identified goals of Appellant's invention.

For these reasons, Meisner does not disclose each and every element of the invention set forth in claims 2, 3, 8, and 10. Claims 2, 3, 8, and 10 are therefore not anticipated by Meisner, and this ground of rejection should therefore be reversed.

B. Rejection Under 35 U.S.C. § 103(a), Meisner, Taken with Joullie et al. and Chemical Abstracts Registry

Claims 2-8 and 10 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Meisner taken with Joullie et al. and Chemical Abstracts Registry file print.

1. The Law of Obviousness

The PTO bears the burden of establishing a case of prima facie obviousness. In re Fine, 837 F.2d 1071, 1074 (Fed. Cir. 1988). The critical inquiry for obviousness is whether "there is something in the prior art as a whole to suggest the desirability, and thus the obviousness, of making the combination." Fromson v. Advance Offset Plate, Inc., 755 F.2d 1549, 1558 (Fed. Cir. 1985). In other words, obviousness "cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination." In re Fine, 837 F.2d 1071, 1075 (Fed. Cir. 1988), quoting ACS Hospital Systems, Inc. v. Montefiore Hospital, 732 F.2d 1572, 1577 (Fed. Cir. 1984). This suggestion cannot stem from the applicant's own disclosure, however. In re Ehrreich, 590 F.2d 902 (CCPA 1979).

2. Claims 2-8 and 10

Claim 10 from which claims 2-8 depend, is directed to a method of counter acting the overproduction of nitric oxide, consisting essentially of: administering to a patient a therapeutically effective amount of an S-alkylthiol as an antagonist of S-nitrosothiols. Again, by definition, claim 10 is limited to the administration of an S-alkylthiol and other ingredients that "do not materially affect the basic and novel characteristic(s)" of the claimed invention. MPEP § 2111.03.

As already extensively shown above, Meisner does not teach Appellant's claimed invention since Meisner requires the administration of a precursor or stimulant of epinephrine or nor-epinephrine production selected from tyrosine, and phenylalanine. Since Appellant's invention is aimed at avoiding the side effects of vasoconstrictors, the inclusion of the vasoconstricting agents required by Meisner would "materially affect the basic and novel characteristic(s)" of the claimed invention."

Meisner further does not provide an incentive or motivation for one skilled in the art to alter its teachings to remove the requirement of a precursor or stimulant of epinephrine or nor-epinephrine production. Meisner, in fact, teaches away from its removal in stating that such compounds are necessary for use in promoting proliferation of the type of cell (fibroblasts) which are involved in the healing of periodontal tissue. (Col. 4, lines 33-41).

The addition of the secondary references of Joullie et al. and Chemical Abstracts do not alleviate the missing teachings of the primary reference. The Examiner argues that, "it would have been well within the purview of the skilled artisan to inject the S-methylcysteine composition of Meisner into a patient since as taught by Joullie it is well known to inject S-methyl cysteine for therapeutic purposes." (1/24/05 Office Action, p. 4). Since it has already been established, however, that it is not obvious in view of Meisner to inject an S-

methylcysteine composition into a patient without the co-administration of a vasoconstricting agent, the addition of Joullie and Chemical Abstracts as secondary references to the primary references do not overcome the deficiencies in the Examiner's case for obviousness.

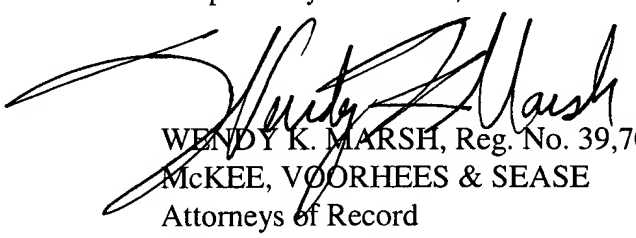
Since the Examiner has failed to establish a prima facie case for obviousness, claims 2-8 and 10 are not rendered obvious by Meisner taken with Joullie et al. and Chemical Abstracts. This ground of rejection should therefore be reversed.

IX. CONCLUSION

For the above-stated reasons, it is submitted that the claims are in a condition for allowability. The decision of the Examiner, therefore, should be reversed and the case allowed.

Enclosed herein please find the Appeal Brief and Request for Oral Hearing in the amount of $750.00 ($250 + $500). If this amount is not correct, please consider this a request to debit or credit Deposit Account No. 26-0084 accordingly.

Respectfully submitted,



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APPENDIX

2. The method of claim 10 wherein the S-alkylthiol is selected from the group consisting of S-ethylcysteine, S-methylcysteine, S-methylcysteamine, S-ethylcysteamine, S-ethylglutathione, S-methylglutathione, S-methylcoenzyme A, and S-ethylcoenzyme A.

3. The method of claim 10 wherein the S-alkylthiol is selected from the group consisting of S-ethyl-L-cysteine, S-methyl-L-cysteine, S-ethylglutathione, S-methylglutathione, S-methylcysteamine, S-ethylcysteamine, S-methylcoenzyme A and S-ethylcoenzyme A.

4. The method of claim 10 wherein the S-alkylthiol is a pharmaceutically acceptable salt form.

5. The method of claim 2 wherein the S-alkylthiol is a pharmaceutically effective salt form.

6. The method of claim 3 wherein the S-alkylthiol is a pharmaceutically acceptable salt form

7. The method of claim 10 wherein administration is intravenously.

8. The method of claim 10 wherein the dose ranges from about 100 mg to about 10 g.

10. A method of counter acting the overproduction of nitric oxide which often occurs in hypotension and shock, consisting essentially of: administering to a patient a therapeutically effective amount of an S-alkylthiol as an antagonist of S-nitrosothiols.